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## Letter to the Editor

**The effect of COVID-19 on parathyroid glands**

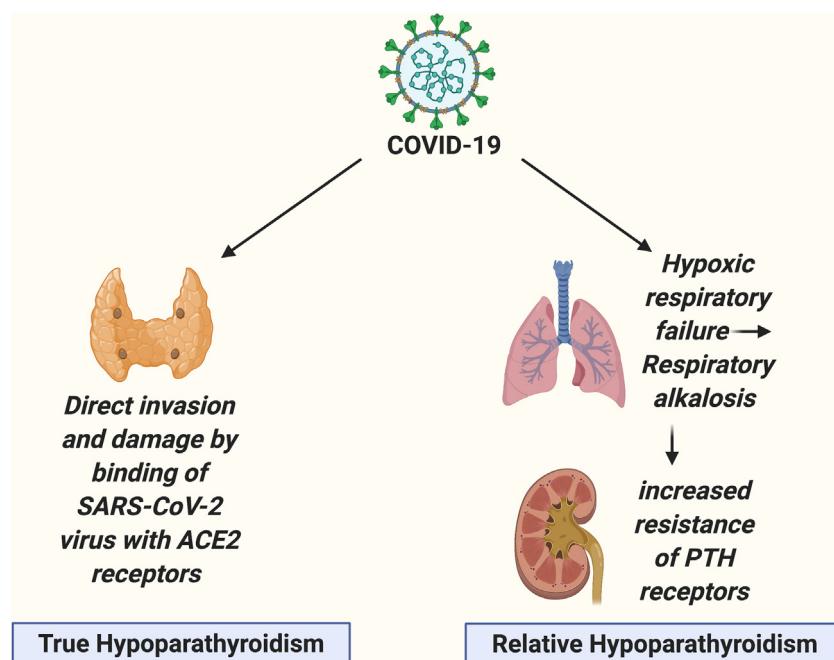
Dear Editor,

We read with great interest the research article of Liu et al. who found that almost two third of patients with novel coronavirus disease (COVID-19) had hypocalcaemia [1]. Few mechanisms which explain the causes of hypocalcaemia in COVID-19 have been discussed, such as vitamin D deficiency, hypoalbuminemia, impaired intestinal absorption of calcium, hypoxic tissue damage with subsequent increase in calcium influx and impaired secretion of and response to parathyroid hormone (PTH) secondary to increased levels of inflammatory cytokines [1]. We would like to add another two possible mechanisms which discuss the possible effects of COVID-19 on parathyroid glands that could improve our understanding of the possible link between this disease and hypocalcaemia.

To date, little is known about the effect of the novel coronavirus (SARS-CoV-2) on parathyroid glands. Elkattawy et al. reported a 46-year-old patient admitted with severe COVID-19 infection and had a prolonged hospital stay. His laboratory workup showed hyperphosphatemia and low parathyroid hormone level. All possible causes of hypoparathyroidism have been excluded. To the best of our knowledge, this is the first and the only report in the literature so far which stated that COVID-19 can be considered

as a possible direct cause of hypoparathyroidism [2]. Because of the limited data which link between SARS-CoV-2 and parathyroid glands, going back to the studies which were conducted on the previous generation of coronavirus (SARS-CoV), the culprit of severe acute respiratory syndrome (SARS) epidemic in 2003, could improve our understanding of this topic. Tissue samples taken from patients died of SARS identified SARS-CoV RNA and antigenic materials in parathyroid gland acidophilic cells [3]. In addition, Increased expression levels of angiotensin converting enzyme 2 (ACE2) receptors were detected in acidophilic cells of parathyroid glands [4]. Therefore, SARS-CoV-2 might have the potential to directly invade the parathyroid glands by binding with acidophilic cells ACE2 receptors. This could explain the finding of hypoparathyroidism in the COVID-19 patient reported by Elkattawy et al.

As we all know, the main cause of hospital admission in patients with COVID-19 is hypoxic respiratory failure which requires respiratory support, including oxygen therapy, intensive care unit admission and mechanical ventilation. Tachypnoea and increased work of respiration causes carbon dioxide washout which leads to respiratory alkalosis. Interestingly, A clinical study showed that chronic respiratory alkalosis increases resistance of renal parathyroid hormone receptors to PTH, leading to hypocalcaemia and hyperphosphatemia [5]. However, no increase in PTH level was detected despite progressive hypocalcaemia, which could



**Fig. 1.** The possible effects of COVID-19 on parathyroid glands (created with [biorender.com](https://biorender.com)).

indicate that chronic respiratory alkalosis might lead to relative hypoparathyroidism [5]. Therefore, we can conclude that COVID-19 could affect the function of parathyroid glands indirectly secondary to its effect on the respiratory system.

In conclusion, Covid-19 might affect the function of parathyroid glands by two possible ways; directly through invasion of parathyroid gland tissues by SARS-CoV-2 virus, and indirectly secondary to respiratory failure and chronic respiratory alkalosis (Fig. 1), which can be considered as additional mechanisms explain the prevalence of hypocalcaemia in patients with COVID-19. However, these conclusions might not be entirely accurate as they are drawn from very limited, non-high-quality data, especially when reviewing the human protein atlas database which showed that there is no ACE2 expression in parathyroid tissues, which contradicts He et al.'s findings [6]. Therefore, we think that more research is required to enhance our understanding in this area, giving the fact that hypocalcaemia has become a frequent biochemical finding in patients with COVID-19.

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## Competing interests

None declared.

## Ethical approval

Not required.

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